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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,950	03/19/2004	Christine Konradi	04843/120003	8080

21559 7590 01/08/2009

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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
01/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/804,950	KONRADI ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 39-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 39-41* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 9/29/2008.

2. Currently Claims 1-2 and 39-41 are pending. Claims 3-38 have been cancelled.

3. The following rejections are reiterated or newly applied. Specifically the 35 USC 103(a) of Smeitink et al. in view of Lockhart et al. has been newly applied. Response to arguments follows.

4. This action is NonFINAL.

Claim Objections

Claim 2 is objected to because the claim specifically recites nonelected subject matter. The Claims require the analysis of the non-elected nucleic acid molecules. Applicant has elected for examination of the claim in so far as it requires ATP Synthase, F1 complex, 0 subunit; ATP Synthase, F0 complex, d subunit; ATP Synthase, F0 complex, C3 subunit; ATP Synthase, F1 complex, gamma polypeptide 1; ATP Synthase F0 complex subunit F in the reply to restriction (4/20/2006). Prior to allowance of this, the non-elected subject matter will be required to be deleted from the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-2 and 39-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Wallace et al. (US Patent Application Publication US 2006/0099578 May 11, 2006) as evidenced by Wallace (US Patent 5494794 February 27, 1996, referred to as Wallace '794).

With regard to Claim 1, Wallace et al. teaches microarray consisting of probes for mitochondrial genes (abstract). Wallace et al. teaches that these arrays can contain subsets of probes drawn to mitochondrial energy (p. 2 paragraph 10). Wallace et al. teaches that the microarray can be composed of mtDNA genes from NADH, Cytochrome b, Cytochrome c, ATP synthase 6, ATP synthase 8 (Table 1 and p. 3 paragraph 17). Therefore Wallace et al. teaches a microarray comprising nucleic acid molecules which are at least 90% of nucleic acid molecules that encode polypeptides of complex I, II, III, IV, or V (e.g. NADH, Cytochrome b, Cytochrome c, ATP synthase 6, ATP synthase 8). Wallace et al. teaches that the arrays can be designed such that genes related to OXPHOS are detected (p. 9 paragraph 64).

OXPHOS is composed of 5 enzyme complexes assembled from 13 mitochondrial DNA and 50 nuclear DNA subunits (as evidenced by Wallace '794 Column 1 lines 60-67). Wallace '794 teaches that OXPHOS is composed of Complex I (NADH); complex III (cytochrome c and cytochrome b); Complex IV (cytochrome c, COI, COII, COIII); and complex V (ATP synthase) (as evidenced by Wallace '794 Column 1 lines 60-67 and

Column 2 lines 1-5). Therefore an array related to OXPHOS would include nucleic acid molecules of mitochondrial respiratory chain of complex I, III, IV, and V.

With regard to Claim 2, Wallace et al. teaches the array can include any number of genes related to mitochondrial function including ATP Synthase, F1 complex, 0 subunit; ATP Synthase, F0 complex, d subunit; ATP Synthase, F0 complex, C3 subunit; ATP Synthase, F1 complex, gamma polypeptide 1; ATP Synthase F0 complex subunit F (Table 3).

With regard to Claim 39, Wallace et al. teaches that the probes are 20-30 nucleotides in length (p. 4 paragraph 24).

With regard to Claims 40-41, Wallace et al. teaches the microarray can contain probes for all genes involved in mitochondrial biology or can contain probes for at least 10 genes or at least 25 genes (p. 6 paragraph 42).

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply asserts that the polypeptides forming complexes I-V of the mitochondrial respiratory chain are made up of polypeptides coded for by both nucleotide genes and mitochondrial genes (p. 5 2nd paragraph). The reply asserts that the genes listed in Table 1 are naturally coded for by the mitochondrial genome, whereas the claim requires the nucleotide acid molecules of the array to encode polypeptides that are naturally coded for by nucleotide genes (p. 5 3rd paragraph). The

reply asserts that the OXPHOS polypeptides code for both nuclear genes and mitochondrial genes, however, Claim 1 requires that at least 90% of the nucleic acid molecules bound to the array be nuclear encoded genes that encode a polypeptide of Complex I, II, III, IV, or V (p. 5 last paragraph). The reply asserts that fewer than 90% of the polypeptides of complexes I-V are coded fro nuclear genes and therefore the mere disclosure of OXPHOS genes cannot anticipate the claim (p. 5 last paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply seems to be asserting that there is a structural difference between the claimed nucleic acid and the nucleic acids taught by the Wallace reference because the genes listed in Table 1 are coded for by the mitochondrial genome and nuclear genes and therefore are not limited a microarray consisting of at least 90% of nucleic acid molecules encoding polypeptides being naturally coded for by a nuclear gene. The reply asserts that the claimed array is limited to nucleic acid molecules that are at least 90% nucleic acid molecules that encode polypeptides being naturally coded for by a nuclear gene. However, the claimed microarray is not limited to at least 90% of nucleic acid molecules that encode polypeptides naturally coded for by a nuclear gene, but rather the microarray consists of a solid support onto which at least two nucleic acid molecules are bound wherein at least 90% of the at least two nucleic acid molecules are nucleic acid molecules that encode polypeptides naturally coded for by a nuclear gene. It is suggested that the claim be amended to “a microarray consisting of at least two nucleic acid molecules…” to limit the scope of the claim to microarray with 90% nucleic acid molecules that encode polypeptides being naturally coded for by a nuclear gene.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US Patent 5494794 February 27, 1996) in view of Lockhart et al. (US Patent 6040138 March 21, 2000).

With regard to Claim 1, Wallace teaches probes to detect mutations in mitochondrial DNA (abstract). Wallace teaches defects in OXPHOS may play a role in the pathogenesis of Alzheimer's disease and Parkinson's disease (column 1 lines 39-

41). Wallace teaches OXPHOS is composes of 5 enzyme complexes assembled from 13 mitochondrial DNA and 50 nuclear DNA subunits (Column 1 lines 60-67). Wallace 'teaches that OXPHOS is composes of Complex I (NADH); complex III (cytochrome c and cytochrome b); Complex IV (cytochrome c, COI, COII, COIII); and complex V (ATP synthase) (Column 1 lines 60-67 and Column 2 lines 1-5). Wallace teaches the design of probes for the detection of these regions (Column 7 lines 25-45). Therefore Wallace teaches probes related to OXPHOS which would include nucleic acid molecules of mitochondrial respiratory chain of complex I, III, IV, and V.

With regard to Claim 39, Wallace teaches that these probes can be 40 nucleotides in length (Column 7 lines 39-41).

Wallace et al., however, does not teach placing the mitochondrial respiratory chain probes on an array.

Lockhart et al. teaches placing oligonucleotides probes onto an array (solid support) to detect expression (Abstract).

With regard to Claims 40-41, Lockhart et al. teaches that the array of probes can comprise up to 100 different oligonucleotide probes (abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to bind the probes of mitochondrial respiratory chain as taught by Wallace onto the array taught by Lockhart et al. with a reasonable expectation of success. The ordinary artisan would want to incorporate the probes onto the array because Lockhart et al. teaches that probes on an array can be used to detect a large number of different target nucleic acids at once and determine the relative

abundance of each in a sample (Column 2 lines 35-55). Therefore the ordinary artisan would be motivated to place the probes onto an array in order to detect quickly expression changes in a large number of probes in order to quickly determine changes in the OXPHOS.

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply asserts that the '794 (Wallace et al.) patent and the '138 patent fail to teach an array where 90% of the nucleic acids encode polypeptides of complex I-V of the mitochondrial respiratory chain which are naturally coded for by nucleotide genes (p. 6 3rd paragraph). The reply asserts that '794 patent discloses detecting mutations in mitochondrial genes for diagnosis of disease but is silent with respect to nuclear genes involved in the mitochondrial respiratory chain (p. 6 last paragraph). The reply asserts that because the nucleic acid molecules recited in claim 1 encode polypeptides naturally coded for by nucleotides genes the '794 patent fails to teach this claim limitation (p. 6 last paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply seems to be asserting that there is a structural difference between the claimed nucleic acid and the nucleic acids taught by the Wallace reference because the genes listed in Table 1 are coded for by the mitochondrial genome and nuclear genes and therefore the structure taught by Wallace is not limited to a microarray consisting of at least 90% of nucleic acid molecules encoding polypeptides being naturally coded for

by a nuclear gene. The reply asserts that the claimed array is limited to nucleic acid molecules that are at least 90% nucleic acid molecules that encode polypeptides being naturally coded for by a nuclear gene. However, the claimed microarray is not limited to at least 90% of nucleic acid molecules that encode polypeptides naturally coded for by a nuclear gene, but rather the microarray consists of a solid support onto which at least two nucleic acid molecules are bound wherein at least 90% of the at least two nucleic acid molecules are nucleic acid molecules that encode polypeptides naturally coded for by a nuclear gene.

Wallace et al teaches that the OXPHOS complex comprises 13 mtDNA and 50 nuclear DNA subunits and therefore teaches genes that are from the nuclear gene are part of the OXPHOS complex which can be detected.

12. Claims 1, 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seitink et al. (Human Molecular Genetics 1998 Vol. 7 p. 1573) in view of Lockhart et al. (US Patent 6040138 March 21, 2000).

With regard to Claim 1, Smeitink et al teaches that complex I of the mitochondrial respiratory chain comprises nucleic genes (abstract). Smeitink et al teaches that mutational analysis of nuclear encoded subunits has enormous implications for genetic counseling (p. 1573 2nd column 1st full paragraph). Smeitink et al. provides the genes of the human nuclear encoded subunits of complex I (Table 1).

Smeitink et al however, does not teach placing the mitochondrial respiratory chain probes on an array.

Lockhart et al. teaches placing oligonucleotides probes onto an array (solid support) to detect expression (Abstract).

With regard to Claim 39, Lockhart et al. teaches the probes can be at least 40 nucleotides in length (column 15 lines 53-60).

With regard to Claims 40-41, Lockhart et al. teaches that the array of probes can comprise up to 100 different oligonucleotide probes (abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to bind the probes of mitochondrial respiratory chain as taught by Smeitink et al onto the array taught by Lockhart et al. with a reasonable expectation of success. The ordinary artisan would want to incorporate the probes onto the array because Lockhart et al. teaches that probes on an array can be used to detect a large number of different target nucleic acids at once and determine the relative abundance of each in a sample (Column 2 lines 35-55). Therefore the ordinary artisan would be motivated to place the probes onto an array in order to detect quickly expression changes in a large number of probes in order to quickly determine changes in the nuclear genes of human complex I.

Conclusion

13. No claims are allowed

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Katherine Salmon/
Examiner, Art Unit 1634

/Ram R. Shukla/

Supervisory Patent Examiner, Art Unit 1634